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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/927,765

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Michael J. Mahan

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07/19/2004

MORRISON & FOERSTER LLP

755 PAGE MILL RD

PALO ALTO, CA 94304-1018

EXAMINER

FIELD, TAMMY K

ART UNIT

PAPER NUMBER

1645

DATE MAILED: 07/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/927,765

Applicant(s)

MAHAN ET AL.

Examiner

Tammy K. Field

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 March 2004.
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.


Disposition of Claims

- 4) ☒ Claim(s) 1-26 and 31-34 is/are pending in the application.
- 4a) Of the above claim(s) 8-13, 23-26, and 31-34 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7 and 14-22 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f). 
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

DETAILED ACTION

Final Action

Remarks

1. The Office acknowledges amendments to the specification reflecting status of parent applications and amended Claims 1, 15, and 18. It is further noted that Applicants have reserved the right to rejoin withdrawn method claims if the pending elected product Claims 1-7, 14-22 with previous species election of *Salmonella* are found allowable.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office Action.

Status of Claim Objections

3. Claim 1 objection due to informalities is withdrawn.

Status of Claim Rejections - 35 USC § 102

4. Rejection of Claims 1-7, 14-19 under 35 U.S.C. 102(e) are maintained as being anticipated by Miller, III, *et al.* (US Patent No. 5,731,196, published March 24, 1998) in light of Heithoff, D.M. *et al.* (Science 284: 967-970).

The evidence of record discloses in applicants' Provisional Applications; 60/183,043 at page 21, line 16 – page 22, line 14 and 60/198,250 at page 21, line 16 – page 22, line 20. The specification of both Provisional Applications disclose that “*Salmonella* pathogenesis is known to be controlled by PhoP, a DNA binding protein”. Results of regulatory studies disclosed by applicants further disclose that both “DAM and PhoP constitute an overlapping global regulatory network controlling *Salmonella* virulence”. Since there is a close overlapping relationship between PhoP and DAM regulatory genes, inherently alterations of the *Salmonella* genome affecting virulence in PhoP are anticipated in the instant invention.

Miller, III *et al.* teach in preferred embodiments a bacterial cell, *e.g.* *S. typhi* including a virulence attenuating mutation in a gene regulated by a phoP regulatory system (instant Claims 1-7) in a vaccine composition at column 2, line 52 – column 3, line 51. Miller, III *et al.* further teach a mutation attenuates virulence if, as a result of the mutation, the level of virulence of the mutant cell is decreased in comparison with the level of parent strain (instant Claim 19) at

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column 5, lines 57-60. Miller, III *et al.* also teach a live Salmonella vaccine, as used herein, is a preparation including material that evokes a desired biological response, *e.g.* an immune response, in combination with a suitable carrier (instant Claims 1-7, 14, and 15-18) at column 5, line 39.

Inherently Miller, III *et al.* anticipates the now claimed invention. Atlas Powder Co. V IRECA, 51 USPQ2d 1943, (FED Cir 1999) states, "Artisans of ordinary skill may not recognize the inherent characteristics of functioning of the prior art...However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discover". The Court further held that "this same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art".

Miller, III *et al.* thus anticipates the instantly claimed invention.

Applicants submit that DAM does not significantly affect expression of all PhoP activated genes and while PhoP may affect DNA methylation activity, this regulation does not occur at the transcriptional level since Dam does not alter PhoP expression, nor does PhoP alter Dam expression.

Applicants arguments received March 22, 2004 have been carefully considered but they are not found persuasive. The Examiner respectfully acknowledges the amendment to independent Claims and although the Examiner appreciates the specific Specification disclosures, Applicants have not shown with certainty why the mutations in Miller, III *et al.* reference does not anticipate the instant claimed invention. Further, the teachings of Heithoff, D.H. *et al.* **do** (emphasis added) indicate Dam activity of Salmonella regulates the expression of at least 20 genes known to be induced during infection (inherently at the transcriptional level) wherein a subset of these genes are among those activated by the PhoP global virulence sites, as evidenced by alterations in DNA methylation patterns (Abstract) and more specifically taught at Fig. 2 at page 968. Therefore, it appears without evidence to the contrary that PhoP mutations do inherently disclose the claimed invention.

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5. Claims 1-7, 14-18, and 22 under 35 U.S.C. 102(e) are maintained as being anticipated by Miller *et al.* (US Patent No. 5,843,426, published December 1, 1998) in light of Heithoff, D.M. *et al.* (Science 284: 967-970).

Miller *et al.* teach a Salmonella vaccine, the invention features a bacterial cell, preferably a Salmonella cell, e.g. *S. typhi* (instant Claims 6-7) the virulence of which is attenuated by a first mutation in a phoP region (instant Claims 1- 5), where said bacterial cell can be used as a vaccine to immunize a mammal against salmonellosis (instant Claims 14-18) at column 2, line 65 – column 3, line 11. Miller *et al.* also teach that constitutive expression of phoP (instant Claim 22) is the result of a change or mutation in the phoP regulatory region at column 3, lines 35-41.

The reference thus anticipates the instantly claimed invention.

Applicants urge that independent Claims 1, 15, and 18, as amended, specifically where the alteration of Dam activity is caused by altering expression of the Dam gene or mutating the Dam gene and further indicated by the disclosure of the specification state that PhoP does not affect Dam expression and therefore, bacteria with mutated PhoP do not anticipate the present invention.

Upon further consideration of applications arguments and in light of the teachings of Heithoff, D.M. *et al.*, the Examiner respectfully submits Miller *et al.* anticipates the claimed invention for the same reasons provided supra in that without evidence to the contrary PhoP mutations do inherently disclose the claimed invention.

6. Claims 1-7, 14-22 under 35 U.S.C. 102(b) are maintained as being anticipated by Miller, S.I. and Mekalanos, J.J. 1990. (J. Bacterio. 172(5): 2485-2490) in light of Heithoff, D.M. *et al.* (Science 284: 967-970).

Miller, S.I. and Mekalanos, J.J. teach a composition comprising a pharmaceutically acceptable excipient and attenuated *S. typhimurium* at pages 2485-2486 (also see Table 1). Miller, S.I. and Mekalanos, J.J. also teach attenuated *S. typhimurium* is an immunogenic composition when mice previously used for live vaccine inoculation of attenuated *S. typhimurium* survived oral challenge experiments at page 2486 at Table 2. Miller, S.I. and

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Mekalanos, J.J. further teach a *phoP* locus mutation (*pho-24*) results in constitutive expression of genes activated by the PhoP-PhoQ two-component regulatory system and in attenuation of virulence and survival within cultured macrophages at 2488, Figure 3. Miller, S.I. and Mekalanos, J.J. incorporate thought reference, Miller, S.I. et al. 1989 Proc. Natl. Acad. Sci. USA 86: 5054-5058 that null mutations in *phoP* and *phoQ* decrease the expression of the same genes whose expression is derepressed by the *pho-24* mutation and it is apparent that mutations that inactivate or activate the PhoP-PhoQ regulation can attenuate virulence at page 3488.

The reference thus anticipates the instantly claimed invention.

Since the office does not have the facilities for examining and comparing applicants' detection and diagnosis methods with the methods disclosed in the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed method and the methods of the prior art (*i.e.* that the methods of the prior art does not possess the same material structural and functional characteristics of the claimed methods). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald et al.*, 205 USPQ 594.

Applicants urge that Miller and Mekalanos do not disclose bacteria with altered Dam expression or Dam mutations for the same reasons as set forth supra. It is the Examiners position that Miller and Mekalanos anticipates the claimed invention for the same reasons provided supra and in light of the teachings of Heithoff, D.M. *et al.* in that without evidence to the contrary *PhoP* mutations do inherently disclose the claimed invention.

Double Patenting

7. Claims 1-7 and 14-22 rejection under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-46 of copending Application No. 09/928,227 (Pregrant Publication 2002/0086332 A1) is maintained.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the instant application and the copending application ('227) are both drawn to a composition of bacteria with altered DNA adenine methylase (Dam) activity.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

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Applicants submit that should the present claims in the co-pending application be found allowable, Applicants will file a terminal disclaimer. It appears there has not been a terminal disclaimer filed at the time of this response.

8. Claims 1-7 and 14-22 provisional rejection under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-29 of copending Application No. 09/927,788 (Pregrant Publication 2002/0081317 A1) is maintained.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the instant application and the copending application ('788) are both drawn to an immunogenic composition of bacteria with altered DNA adenine methylase (Dam) activity by a heterologous nucleotide.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicants submit that should the present claims in the co-pending application be found allowable, Applicants will file a terminal disclaimer. It appears there has not been a terminal disclaimer filed at the time of this response.

Status of the Claims

9. No claims are allowed.

Conclusion

10. The prior art of record and not relied upon is considered pertinent to applicant's disclosure:

- a. Curtiss, III *et al.* US Patent No. 5,424,065, published June 13, 1995. Vaccines containing avirulent PHOP-Type microorganisms.

11. Applicant's amendment necessitated maintaining prior rejections and re-direction of new grounds of rejection necessitated by amendment presented in this Office Action. Accordingly,

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THIS ACTION IS MADE FINAL. See MPEP 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

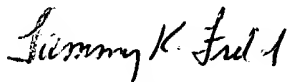
12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tammy K. Field whose telephone number is (571) 272-0856. The examiner can normally be reached on Monday-Friday from 7am-4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached at (571) 272- 0864.

Papers relating to this application may be submitted to Technology Center 1600 Group 1640 by facsimile transmission. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306 for regular communications and After Final communications.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov/>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Tammy K. Field

July 13, 2004